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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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BANNER & WITCOFF
1001 G STREET N W
SUITE 1100
WASHINGTON, DC 20001

EXAMINER	
PONNALURI, PADMASHRI	
ART UNIT	**PAPER NUMBER**
1639	

DATE MAILED: 06/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/726,624	LI, MIN	
	Examiner	Art Unit	
	Padmashri Ponnaluri	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 March 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5,9,17,22,45-51,53-63 and 65-75* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 5, 9, 17, 22, 45-51, 53, 55-56, 58-63, 65, 67-68, 70-75* is/are rejected.

7)☒ Claim(s) *54,57,66 and 69* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The response filed on 3/29/04 has been fully considered and entered into the application.

2. Claims 1, 5, 9, 17, 22, 45-51, 53-63, and 65-75 are currently are being present in this application.

3. In the previous office action mailed on 11/4/03, claims 54, 57, 66, 69 were not addressed. Examiner apologizes for inadvertently missing to indicate the status of these claims in the previous office action. However, the subject matter of these claims was indicated allowable.

Maintained Claim Rejections

4. The new matter rejection of claims set forth in the previous office action mailed on 11/4/03 has been maintained for the reasons of record.

5. The written description rejection set forth in the previous office action mailed on 11/4/03 has been maintained for the reasons of record.

6. The art rejection of claims 1, 5, 9, 45-51, 53, 55-56 over Schatz et al, set forth in the previous office action mailed on 11/4/03 has been maintained for the reasons of record.

7. The art rejection of claims 1, 5, 9, 17, 22, 45-51, 53, 55-56, 58-63, 65, 67-68 over Schatz et al and Barbas III, set forth in the previous office action mailed on 11/4/03 has been maintained for the reasons of record.

Response to Arguments

8. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

9. Applicant's arguments filed on 3/29/04, regarding the written description rejection have been fully considered but they are not persuasive.

Claims 1, 5, 7, 9, 17, 22, 45-51, 55-56, 58-63, 67-68 and 70-75are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection..

The instant claims briefly recite a method of detecting the presence of a polypeptide in a sample comprising contacting the sample with a homogenous population of a detectable virus expressing on its surface a ligand for the polypeptide and detecting the binding of the virus to the sample.

The specification discloses NMDA as the polypeptide in the sample and the ligands for the polypeptide in the sample is Mag -4.1 or Mag -4.2, which are known to be the ligands for the specific polypeptide. Thus in the claimed method a known pair of ligand and polypeptide are used. The specification disclosure of use of Mag proteins in identifying NMDA receptors in the sample clearly do not provide an adequate representation regarding the open ended claimed method of identifying the presence of any polypeptide in a sample as in the presently claimed invention.

The specification discloses recombinant bacteriophage cells expressing the fusion proteins of the ligands (Mag proteins) and coat proteins on the surface, and use of the bacteriophage in detecting specific NMDA proteins in the sample, which meets the written description. However, the instant claims are open to the use of any viral vectors, however the specification discloses only the use of bacteriophage and pVIII coat protein to express the fusion proteins. None of these meet the written description provision of 35 U.S.C 112, first paragraph. The specification provides insufficient written description to support the genus encompassed by the claim.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.).

With the exception of bacteriophage expressing the fusion proteins of pVIII coat protein and Mag proteins, and the use of the bacteriophage expressing the fusion proteins in the method of detecting the NMDA receptors in the sample, the skilled artisan cannot envision the method of using the other viral vectors and use of the viral

vectors in detecting any other proteins in the sample. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.* , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli* , 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood* , 107 F.3d at 1572, 41 USPQ2d at 1966.

Therefore, only bacteriophage vectors expressing the Mag proteins as fusion proteins and use of the bacteriophage vectors in the method of detecting NMDA receptors, but not the full breadth of the claim meet the written description provision of 35 U.S.C 112, first paragraph.

Applicants argue that 'why one of ordinary skill in the art would not be able to recognize that any virus, ligand, or means of viral surface expression could be used. Information which is well known in the art need not be described in detail in the specification. The Patent Office has not presented any reasons why any of the known viruses, ligands, or means of expressing on virus surface could not be used.'

Applicant's arguments have been fully considered and are not persuasive.

The instant claim is drawn to 'a method of detecting the presence of a polypeptide in a sample comprising contacting the sample with a homogenous population of a detectable virus

expressing on its surface a ligand for the polypeptide and detecting the binding of the virus to the sample.' And claim 5 recites that ' a selected polypeptide in a sample', and 'a ligand previously demonstrated to specifically bind the selected polypeptide.' Thus, the instant claimed methods are drawn to the use of previously known ligand and target which interact with each other. The specification discloses NMDA as a polypeptide in the sample and the ligand is Mag –4.1 or Mag 4.2, which are known as specific binding pairs.

"[T]he essential goal' of the description of the invention requirement is to clearly convey the information that an applicant has invented the subject matter which is claimed." In re Barker, 559 F.2d 588, 592 n.4, 194 USPQ 470, 473 n.4 (CCPA 1977). Another objective is to put the public in possession of what the applicant claims as the invention. See Regents of the University of California v. Eli Lilly, 119F.3d 1559, 1566, 43 USPQ2d 1398, 1404 (Fed. Cir. 1997), cert. denied, 523 U.S. 089 (1998).

The instant claimed method is drawn to a general method of screening for the presence of a polypeptide in a sample by contacting the sample with a homogenous population of virus expressing on its surface a ligand for the polypeptide. There is no relationship between the ligand expressed on the virus and the sample or the characteristics of the ligand and the polypeptide are not recited in the claim . Without the prior knowledge of the ligand and the polypeptide present in the sample, the skilled in the art would not known which ligand to be used in the claimed method.

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice

or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus (see i)(C), above). See Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406.

A "representative number of species" means that the species which are adequately described are representative of the entire genus. For inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus. See, e.g., Eli Lilly. If a representative number of adequately described species are not disclosed for a genus, the claim to that genus must be rejected as lacking adequate written description under 35 U.S.C. 112, para. 1.

Thus, the instant specification does not disclose a representative number of species (NMDA and MAG- 4.1 or Mag –4.2 are considered as species) representing the genus (polypeptide and ligand). And the specification teaches that the specific binding pairs or receptor-ligands are selected by screening random libraries to identify binding pairs which are used in the claimed method.

Applicants argue that 'the generic scope of the invention is further supported in the disclosure of the individual components utilized in the claimed method. ***The virus disclosed can be any virus: the virus utilized in the method can be a bacteriophage, for example the bacteriophage can be bacteriophage f1, M113 and other bacteriophages known in the art.'***

Thus, the instant specification preferred embodiment is bacteriophage, and the specification

does not teach the use of other virus in the claimed method. Thus, the rejection of record has been maintained for the reasons of record.

10. Applicant's arguments filed on 3/29/04, regarding the new matter rejection have been fully considered but they are not persuasive.

Applicants argue that 'the use of a homogenous population of virus expressing on its surface a ligand for the polypeptide is amply supported throughout the specification as whole.' And applicants point out that in page 3, lines 18-21, 'phage clones with specific interacting peptides from random peptide libraries have been isolated', which indicates the virus population has random peptides, and is not a homogenous population of detectable virus as in the instant claims.

The specification page 11, disclosure does not support the 'homogenous population of detectable virus' as in the instant claims.

The specification page 12, disclosure (the examples herein show the isolation ***of a phage clone*** *carrying a low affinity peptide.....) does not support the '***homogenous population*** *of detectable virus' as in the instant claims.*

The specification page 12, disclosure ('monitoring receptor expression using ***recombinant bacteriophage*** *with specific peptide ligands') does not support the 'homogenous* ***population of*** *detectable virus' as in the instant claims.*

The specification page 14, disclosure ('after five consecutive rounds of selection and amplification, clones that specifically bind N-NR1 fusion protein were identified...') does not support the 'homogenous population of detectable virus' used in the instant claimed method. The specification page 14 description is directed to panning method, which is different from the

claimed method. If applicants mean that the 'a population of detectable virus expressing the specific peptide ligand is identified by multiple rounds of iterative screening or panning, and the identified virus expressing one specific peptide (not the virus expressing the random peptides) prior to the claimed method, applicants are requested to amend the claims. However, applicants are required to show the support in the originally filed specification or the original claims.

11. Applicant's arguments filed on 3/29/04, regarding the rejection of claims over Schatz (US Patent 5,270,170) have been fully considered but they are not persuasive.

Claims 1, 5, 9, 45-51, 53, 55-56 are rejected under 35 U.S.C. 102(b) as being anticipated by US Patent 5,270,170 (Schatz et al).

The instant claims briefly recite a method of detecting the presence of a polypeptide in a sample comprising contacting the sample with a detectable virus expressing on its surface a ligand for the polypeptide and detecting binding of the virus to the sample.

US Patent 5,270,170 teaches peptide libraries and screening method. The reference teaches that the screening method of the invention comprises lysing the cells transformed with the peptide library, contacting the fusion proteins of the peptide library with a receptor and isolating the vector that encodes the peptide that binds to the receptor. The reference also teaches the use of fluorescence-activated cell sorter to identify the peptide. The reference teaches once a peptide ligand of interest has been identified, a variety of techniques can be used to diversify a peptide library to construct ligands with improved properties (see column 15). The reference teaches that the degenerate oligonucleotides encoding the ligand are cloned into the random peptide library expression vector to produce variations of starting peptide sequences, and the method is useful for expanding diversity (see column 15) (refers to the instant claim 5). The reference teaches that the receptor (polypeptide of the instant claims) refers to a molecule that has affinity for a given ligand, and the receptor can be a naturally occurring and can be in an unaltered state or as aggregates with other species (see column 4) (refers to the sample of the instant claims). The reference further teaches that sera, fluids, tissues or cell from patient with disease can be used in the present screening method to identify peptides (see column 5). The reference clearly anticipates the claimed invention.

Applicants argue that Schatz does not employ a homogenous population of virus expressing a ligand on its surface. As discussed supra, the specification as originally filed has no support for the use of homogenous population of detectable virus expressing on its surface a ligand in the claimed method.

And further applicants argue that Schatz does not employ a detectable virus expressing a ligand on its surface. Schatz cited as teaching the use of plasmids or phage vectors which express fusion products.

Applicant's arguments regarding the 'homogenous population of virus expressing on its surface a ligand...' have been fully considered and are not persuasive, since the limitation has been considered as new matter. And further even if the new matter issue has been decided, the reference teaches by repetition of the affinity selection process one or more times, the vectors encoding the peptides of interest can be enriched, thus the reference teaches homogenous population of vectors.

Applicant's arguments have been fully considered and are not persuasive, since the Schatz teach the use of plasmids or ***phage vectors*** *which express fusion products in the screening methods. The specification in page 7 discloses that the 'virus utilized in the method can be a bacteriophage. Thus the reference phage refers to the virus of the instant claims. And further the specification discloses that 'a detectable virus or phage is one that can be detected by any of many possible means. For example, the phage or virus can be detected by a polyclonal or monoclonal antibody directed against the virus ....'. Thus, the reference is teaching the detectable virus.*

Applicants argue that Schatz does not teach the steps of 'contacting a virus with a sample and detecting the presence of a polypeptide in the sample by virus binding to the sample.' Schatz teach the screening method in which the fusion proteins bound to the vectors are contacted with a receptor (i.e., see column 5). Thus the reference is teaching contacting a virus with a sample and detecting the presence of a polypeptide in the sample by virus binding to the sample. Further the reference teaches that the receptor can be aggregate with other species or sera, fluid, tissue or cells from patients with disease can be used in the reference screening method. Thus, the reference clearly teach all the limitations of the claimed inventions, and the rejection of record has been maintained for the reasons of record.

12. Applicant's arguments filed on 3/29/04, regarding the rejection of claims over the combination teachings of Schatz (US Patent 5,270170) and Barbas III (US Patent 6,242,568) have been fully considered but they are not persuasive.

Claims 1, 5, 9, 17, 22, 45-51, 53, 5556, 58-63, 65, 67-68 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 5,270,170 (Schatz et al) and Barbas, III et al (US Patent 6,242,568, filing date 01/1998) in view of the specification disclosure.

Schatz et al has been discussed supra.

The claimed invention differs from the prior art teachings by reciting bacteriophage expressing more than 10 copies of the ligand on its surface. Schatz et al do not teach that more than 10 copies of ligand are displayed on the surface of the phage. However, Barbas, III et al teach that mature phage contain 2500 to 3000 copies of VIII coat protein. And the instant specification discloses that the ligand can be encoded by pIII or pVIII coat protein which is standard in the art. Thus, it would have been obvious to one skilled in the art at the time the invention was made to use to make fusion proteins of ligand linked to pVIII coat protein of a bacteriophage, such that multiple copies upto 3000 copies of the ligand are displayed on the surface of the phage.

Applicants argue that Schatz does not teach the 'homogenous population of detectable

virus expressing a ligand on its surface.' Moreover, Barbas, III teach that pVIII coat protein is expressed in multiple copies.

Applicant's arguments regarding the 'homogenous population' have been fully considered and are not persuasive for the reasons discussed supra. And In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See In re Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); In re Merck & Co., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Schatz teach the use of bacteriophage vectors in screening for the polypeptide in the sample, and Barbas III teach pVIII coat protein in the fusion. Thus, the combined teachings of the references Schatz and Barbas, IIII clearly read on the claimed method.

Allowable Subject Matter

13. Claims 54, 57, 66 and 69 would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112, second paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

Conclusion

14. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Padmashri Ponnaluri whose telephone number is 571-272-0809. The examiner is on Increased Flex Schedule and can normally be reached on Monday through Friday between 7 AM and 3.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

PADMASHRI PONNALURI
PRIMARY EXAMINER

Padmashri Ponnaluri
Primary Examiner
Art Unit 1639